

**Translation**

**PATENT COOPERATION TREATY**

**PCT**

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>B20-01PCT</b>	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. <b>PCT/JP2004/009861</b>	International filing date (day/month/year) <b>02.07.2004</b>	Priority date (day/month/year) <b>03.07.2003</b>
International Patent Classification (IPC) or national classification and IPC <b>A61K45/00 , 31/7056, A61P35/00</b>		
Applicant <b>JAPAN SCIENCE AND TECHNOLOGY AGENCY</b>		

1.	This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.	
2.	This REPORT consists of a total of <u>9</u> sheets, including this cover sheet.	
3.	This report is also accompanied by ANNEXES, comprising:	
a.	<input checked="" type="checkbox"/> (sent to the applicant and to the International Bureau) a total of <u>4</u> sheets, as follows: <input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.	
b.	<input checked="" type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) <u>1 flexible disk</u> , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).	
4.	This report contains indications relating to the following items:	
	<input checked="" type="checkbox"/> Box No. I	Basis of the report
	<input type="checkbox"/> Box No. II	Priority
	<input checked="" type="checkbox"/> Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
	<input type="checkbox"/> Box No. IV	Lack of unity of invention
	<input checked="" type="checkbox"/> Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
	<input type="checkbox"/> Box No. VI	Certain documents cited
	<input type="checkbox"/> Box No. VII	Certain defects in the international application
	<input type="checkbox"/> Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This report is based on translations from the original language into the following \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
    - ☐ international search (Rule 12.3 and 23.1(b))
    - ☐ publication of the international application (Rule 12.4)
    - ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
  - ☐ the international application as originally filed/furnished
  - ☒ the description:
    - pages 1-3, 6-8, 10-23 as originally filed/furnished
    - pages\* 4, 5, 9 received by this Authority on 17.05.2005
    - pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
  - ☒ the claims:
    - nos. \_\_\_\_\_ as originally filed/furnished
    - nos.\* \_\_\_\_\_ as amended (together with any statement) under Article 19
    - nos.\* 2, 3, 5, 6 received by this Authority on 17.05.2005
    - nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
  - ☒ the drawings:
    - sheets fig. 1-9 as originally filed/furnished
    - sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
    - sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
  - ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☒ The amendments have resulted in the cancellation of:
  - ☐ the description, pages \_\_\_\_\_
  - ☒ the claims, nos. 1, 4
  - ☐ the drawings, sheets/figs \_\_\_\_\_
  - ☐ the sequence listing (*specify*): \_\_\_\_\_
  - ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
  - ☐ the description, pages \_\_\_\_\_
  - ☐ the claims, nos. \_\_\_\_\_
  - ☐ the drawings, sheets/figs \_\_\_\_\_
  - ☐ the sequence listing (*specify*): \_\_\_\_\_
  - ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

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## Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 5, 6

because:

☒ the said international application, or the said claims Nos. 5, 6  
relate to the following subject matter which does not require an international preliminary examination (*specify*):

Claims 5 and 6 describe methods of treatment of the human or animal body by surgery or therapy, and thus, pursuant to the provisions of PCT Article 34(4)(a)(i) and PCT Rule 67.1(iv), pertain to subject matter on which this International Preliminary Examining Authority is not required to carry out an international preliminary examination.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 5, 6

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	2, 3	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	2, 3	NO
Industrial applicability (IA)	Claims	2, 3	YES
	Claims		NO

## 2. Citations and explanations (Rule 70.7)

Document 1: H. Bachelez et al., "The use of tetracyclines for the treatment of sarcoidosis," *Archives of Dermatology*, 2001, Vol. 137, No. 1, pages 69-73

Document 2: Tsunaharu Matsushima, "Kansensho no hassho kijo to yobo ni kan suru kenkyu," *Nagasaki Daigaku Nettai Igaku Kenkyusho Kyodo Kenkyu Hokokushu*, 2002, Vol. 2001, pages 62-64

Document 3: Toru Nishiwaki et al., "Kogen keiryu ni yoranai mouse hainikuga shusho model no kaiseki," *Bimansei Hai Shikkan Kenkyuhan, Heisei 14-nendo Kenkyu Hokokusho*, March 2003, pages 186-192

Document 4: L.A. Cone et al., "Cerebral epidural abscess and review of central nervous system infections caused by *Propionibacterium acnes*," *Antimicrobics and Infectious Diseases Newsletter*, 2000, Vol. 18, No. 12, pages 94-95

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Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

Document 5: E. Brauner et al., "Comparative efficacy of trospectomycin (U-63366F), clindamycin, and imipenem against *Bacteroides fragilis* in the infected granuloma pouch model," *Current Therapeutic Research*, 1989, Vol. 45, No. 3, pages 414-20

Document 6: E. Brauner et al., "Comparative study of clindamycin, imipenem, oxacillin and vancomycin in the infected granuloma pouch model," *Journal of Antimicrobial Chemotherapy*, 1989, Vol. 23, No. 6, pages 891-8

Document 1 (see the abstract) cited in the international search report states that tetracycline antibiotics such as minocycline and doxycycline are useful for treating sarcoidosis. Document 1 (see page 72, right column, line 13 to page 73, left column, line 3) also suggests that the efficacy of minocycline and the like against sarcoidosis may derive from the anti-infective effect of tetracyclines against microbes such as *Propionibacterium acnes*.

Document 2 cited in the international search report states that *Propionibacterium acnes* is considered an etiological agent of sarcoidosis, and can cause the formation of granulomas.

Document 3 cited in the international search report indicates that *Propionibacterium acnes* is thought to make induction of granulomas easier and is considered a candidate causative antigen for sarcoidosis, and states

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that pulmonary granulomas are induced by a recurrent immune response to *Propionibacterium acnes*.

Document 4 cited in an earlier written opinion indicates that symptoms of epidural abscess caused by *Propionibacterium acnes* were alleviated following treatment with meropenem (see page 94, right column, lines 9 to 18), and also indicates that *Propionibacterium acnes* is sensitive to antibiotics such as penicillins, cephalosporins, macrolides, meropenem, and clindamycin (page 95, center column, lines 3 to 8).

Document 5 cited in an earlier written opinion indicates the use of antibiotics such as trospectomycin for treating a granuloma pouch caused by infection with *Bacteroides fragilis* (see the abstract).

Document 6 cited in an earlier written opinion indicates the use of antibiotics such as clindamycin for treating a granuloma pouch caused by infection with *Staphylococcus aureus* or *Bacteroides fragilis* (see the abstract).

Claims 2 and 3

Novelty

The invention set forth in the present claims 2 and 3 is not disclosed in any of documents 1 to 6, and thus, said invention is novel.

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Inventive step

Documents 1 to 6

A comparison of the invention disclosed in document 1 and the invention set forth in the present claims 2 and 3 reveals that the two differ in that the invention disclosed in document 1 uses tetracycline antibiotics, whereas the invention according to the present claims 2 and 3 uses other antibiotics such as penicillins.

However, using an antibiotic for which a given microbe has sensitivity to treat a disease wherein said microbe is the predicted etiological agent, as shown in document 4 to 6, is recognized as conventional practice. Concerning this issue, the basis for considering *P. acnes* an etiological agent of sarcoidosis was known at the time of filing, as shown in documents 2 and 3. Further, document 1 specifically indicates that tetracycline antibiotics, for which *P. acnes* has sensitivity, are effective against sarcoidosis, and states that such efficacy may derive from an anti-infective effect against *P. acnes*. In the light of these disclosures, a person skilled in the art could easily take particular notice of the hypothesis that *P. acnes* is an etiological agent of sarcoidosis from among the many hypotheses about the causes of sarcoidosis, and conceive of adapting the invention disclosed in document 1 by using an antibiotic other than a tetracycline against *P. acnes*.

Further, no exceptional effect difficult to predict from documents 1 to 6 is recognized as being produced as a result of such adaptation.

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Therefore, the invention set forth in claims 2 and 3 does not involve an inventive step in the light of documents 1 to 6.

Moreover, in the response to the written opinion, dated 8 September 2005, the applicant asserts that the present invention has an advantageous effect not present in conventional therapeutic agents, but the effect asserted by the applicant results from the use of an antibiotic as an active ingredient, which is recognized as an effect already produced by the invention disclosed in document 1, and not as a new effect produced by replacing the tetracycline antibiotic disclosed in document 1 with another antibiotic.



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## Supplemental Box Relating to Sequence Listing

## Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
- a. type of material
- ☒ a sequence listing
- ☐ table(s) related to the sequence listing
- b. format of material
- ☐ in written format
- ☒ in computer readable form
- c. time of filing/furnishing
- ☐ contained in the international application as filed
- ☒ filed together with the international application in computer readable form
- ☐ furnished subsequently to this Authority for the purposes of search and/or examination
- ☐ received by this Authority as an amendment\* on \_\_\_\_\_
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

\* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."